

THE MERCK INDEX

AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

TWELFTH EDITION

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Published by
Merck Research Laboratories
Division of

MERCK & CO., INC.

Whitehouse Station, NJ

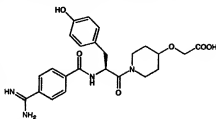
1996



Propionate potassium, $C_{18}H_{15}KO_4$, RS-1988, *Cattley*, mp 190-192°.

THERAP CAT (VET): Growth promotor.

5362, Lamifiban. (S)-[1-[2-[4-(Aminoisinomethyl)-benzoyl]amino]-3-(4-hydroxyphenyl)-1-oxopropyl]-4-piperidinyl]oxy]acetic acid; [1-[N-(4-aminobenzoyl)-1-trycyl]-4-piperidinyl]oxy]acetic acid; RO 44-9883. $C_{24}H_{27}N_3O_5$, mol wt 468.51. C 61.53%, H 4.602%, N 11.96%, O 20.49%. Specific nonpeptide platelet fibrinogen receptor (GP1b/IIla) antagonist. Prep: L. Aliq et al., *Eur. pat. Appl.* 505,868; *idem*, U.S. pat. 5,378,712 (1992, 1995 both to Hoffmann-La Roche); L. Aliq et al., *J. Med. Chem.* 35, 4393 (1992). Pharmacology: J.-P. Carteaux et al., *Thromb. Haemostas* 70, 817 (1993); Y. Takiguchi et al., *ibid.* 73, 683 (1995).



Crystals (zwitterionic form) from water, mp above 200° (dec). $[\alpha]_D^{25} +29.8$ ($c = 0.86$ in 1N HCl).

Trifluoroacetate salt, $C_{24}H_{27}N_3O_5 \cdot C_2F_3O_2$, mp 125-130° (dec). LD₅₀ i.v. in mice: 150 mg/kg (Aliq, 1995).

THERAP CAT: Antithrombotic.

5363, Laminaran. Laminarin. A polysaccharide found in brown seaweed and occurring principally in the *Laminaria* spp. Linear polymer composed of β -D-(1 \rightarrow 3)-linked glucose residues; may contain small amounts of β -D-(1 \rightarrow 6) linkages as interresidue linkages or as branch points and 2-3% D-mannitol as end groups. Two forms of laminaran are recognized; they are referred to as soluble and insoluble laminaran: Percival, *Rosa, J. Chem. Soc.* 1951, 720. Structure: Peat et al., *ibid.* 1958, 724, 729; 1960, 175; Goldstein et al., *Chem. & Ind. (London)* 1959, 124; Annan et al., *ibid.* 1962, 984; Annan et al., *J. Chem. Soc.* 1965, 885; Maeda, Nishizawa, *Carbohydr. Res.* 7, 97 (1968). Structure of soluble laminaran from *Elasmobranchia*: T. Uusi et al., *Acta Biol. Chem.* 43, 603 (1979). NMR studies of laminaran: D. Gagnaire, *Org. Magn. Res.* 11, 344 (1978); H. Friebohn et al., *ibid.* 12, 216 (1979). Review: W. A. P. Black, E. T. Dewar, in *Industrial Gums*, R. L. Whistler, Ed. (Academic Press, New York, 2nd ed., 1973) pp 137-145.

Water-insoluble laminaran, isolated from *L. cloustoni* Edmonstone, *Laminaraceae*, is pptd spontaneously from the acid extract of the plant. Has lower degree of branching than the sol form. Typical analysis of the dry material: 92.5% polyglucose, 0.4% non-volatile matter; $[\alpha]_D^{25} -13.4$ ($c = 0.9$). Amorphous triacetate, $(C_{14}H_{16}O_6)_n$, $[\alpha]_D^{25} -63.5$ ($c = 0.4$ in chloroform).

Soluble form, isolated from *L. digitata*, is separated from the acidified extract only after addition of a precipitant such as ethanol. Typical analysis (on dry basis): 91.2% polyglucose, 1.0% non-volatile matter; $[\alpha]_D^{25} -11.9$ ($c = 2.1$).

Sulfate, *laminaran hydrogen sulfate*. Laminaran can be sulfated to varying degrees. Highly sulfated products have anticoagulant properties comparable to heparin, while laminarans with few sulfate groups are antipneumic only: Besterman, Evans, *Brit. Med. J.* 1957, 1, 310.

5364, Laminin. Abundant structural component of the basal lamina; critical to the stability of the extracellular matrix and to the adhesion of cells to the basement membrane. Family of heteromeric glycoproteins composed of a heavy chain, designated α (also known as A) and 2 light chains, designated β (B1) and γ (B2), which are linked by disulfide bonds to form an asymmetrical cross-shaped structure. Eight genetically distinct laminin subunits have been identified: $\alpha 1, \alpha 2, \alpha 3, \beta 1, \beta 2, \beta 3, \gamma 1$, and $\gamma 2$. Seven different assembly forms (laminins-1 to -7) are known and ap-

pear to be tissue specific and developmentally regulated. Exhibits diverse biological activities. Influences cell growth, morphology and differentiation of a variety of cells via specific receptors including several of the integrins. In murine Engelbreth-Holm-Swarm (EHS) tumor: R. Timpl et al., *J. Biol. Chem.* 254, 9933 (1979). R. Timpl et al., *J. Biol. Chem.* 254, 9933 (1979). R. Timpl et al., *J. Cell Chem.* 27, 317-325 (1985); of role in natural development: Nurcombe, *Pharmacol. Ther.* 56, 247 (1992). Tissue distribution: E. Engvall et al., *Cell Regul.* 1, 731 (1990). β of laminin binding proteins and receptors: R. P. McAnan, *Rev. Cell Biol.* 7, 71-91 (1991); and role in metastasis: V. Castronovo, *Invas. Metast.* 13, 1-30 (1993). Site and function of laminin isoforms: E. Engvall, *Kidn.* 43, 2-6 (1993); K. Tryggvason, *Curr. Opin. Cell Biol.* 1, 882 (1993). Nomenclature: R. E. Burgesson et al., *J. Biol. Med.* 14, 209 (1994). Review of structure: R. Timpl Brown, *ibid.* 275-281.

Laminin-1, EHS-laminin. Prototype laminin pro by murine EHS tumor. Contains $\alpha 1$ (also known as A), $\beta 1$ (B1, B1c) and $\gamma 1$ (B2, B2c) subunits.

Laminin-2, neuron, laminin M. Variant found in muscle, placental trophoblast and Schwann cell basement membranes. Contains $\alpha 2$ (also known as M or Am), $\beta 1$ subunits. Identification: I. Lelov, E. Engvall, *Proc. Acad. Sci. USA* 85, 1544 (1988); K. Ehrig et al., *ibid.* 3264 (1990).

Laminin-3, β -laminin, synaptic laminin. Contains $\alpha 3$ (also known as s or B1s) and $\gamma 1$ chains. Identical neuromuscular junction: D. D. Hunter et al., *Nature* 279 (1989).

Laminin-5, kallinin, nicotin. Contains $\alpha 5, \beta 3$, and $\gamma 1$ units. Isolated from human keratinocytes: P. Rousselle *J. Cell Biol.* 114, 567 (1991).

5365, Lamivudine. (2R,4S)-4-Amino-1-[2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-2-(1H-pyrimidin-2-yl)-2-deoxy-3-thiocytydine; (-)-[2R,5S,2'-thiocytydine 1,3-oxathiolan-5-yl]cytosine, 3'-thia-2',3'-dideoxy-3TC; (-)-NGPB-21; (-)-BCH-189; GR-109714X; $C_9H_{11}N_5O_4S$, mol wt 229.26. C 41.91%, H 4.84, 18.33%, O 20.94%, S 13.95%. Reverse transcriptase inhibitor. Prep: J. A. V. Coates et al., *PCT Int. pat.* 17,159, C.A. 117, 11 (1989) (1991). Synthesis of enantiomer: J. W. Beach et al., *J. Org. Chem.* 57, 2127 (1992). Enantiomer: D. C. Humber et al., *Tetrahedron Lett.* 4523 (1992). Comparative *in vitro* anti-HIV activity: V. Coates et al., *Antiviral Res. Chemother.* 36, 733 (1991). Clinical pharmacokinetics: R. van Loeuwen et al., *Int. J. Clin. Pharmacol. Ther.* 18, 235 (1994).



White solid from methanol/ethyl acetate. $[\alpha]_D^{25} - (c = 1.08$ in methanol). Also reported as crystals boiling ethanol, mp 160-162°. $[\alpha]_D^{25} -135$ ($c = 0$ in methanol).

THERAP CAT: Antiviral.

5366, Lamoparan. Org-10172. Low molecular weight heparinoid derived from porcine intestinal mucosa; m of sulfated glycosaminoglycans with mean mol wt 10,000. Prep: A. L. M. Sanders et al., *Eur. pat.* 66,908; *idem*, U.S. pat. 4,438,108 (1982, 1984 both to Akzo). Exhibits antithrombotic activity comparable to standard heparin but with diminished bleeding risk: D. G. Meuleman et al., *Thromb. Res.* 27, 353 (1982); H. Cate et al., *ibid.* 38, 211 (1985). Preliminary pharmacokinetics and tissue distribution in humans: I. D. Brad et al., *Brit. J. Clin. Pharmacol.* 23, 667 (1987). Ch